

Four New Vaccines for Routine Immunization in India: What About Hemophilus Influenza B and Pneumococcal Vaccine?

Sourabh Paul, Jyotiranjana Sahoo

Department of Community Medicine and Family Medicine, All India Institute of Medical Sciences, Bhubaneswar, Odisha, India

ABSTRACT

Immunization is the process whereby a person is made immune or resistant to an infectious disease, typically by the administration of a vaccine. The Expanded Program on Immunization (EPI) was flagged off in India in 1978. According to the recommendation of National technical advisory group of India (NATGI), Government of India is going to include four new vaccines in the UIP for whole India. The four new vaccines are Inactivated Poliomyelitis Vaccine (IPV) for polio, rota viral vaccine, vaccine against rubella, and Japanese encephalitis vaccine (179 districts in India). Here, authors have tried to show a comparative descriptive analysis of the hemophilus influenza and pneumococcal pneumonia with rota virus, so that in near future Government of India can also consider their inclusion in the national UIP. In India, 39.2% of all diarrheal death are due to rota virus, whereas 0.72 million deaths are due to hemophilus influenza B and 1.3 million are due to pneumococcal pneumonia in <5 years age-group. India's indigenous developed rota viral vaccine's (Rotavac) efficacy is 56% in 1st year compared to H influenza B (Hib) efficacy 95% and PCV13 vaccine "3 + 1" dose efficacy 100% (South Africa). Rotarix incremental cost-effectiveness ratio is US \$21.4 to US \$34 per disability-adjusted life years (DALYs) compared to Hib US \$ 819 per DALYs in India. In case of pneumococcal vaccine, India needs more trails on the serotype specificity, efficacy, and cost-effectiveness but there is enough evidence that hemophilus influenza burden is high in India and the present Hib vaccine is safe and highly effective. In future with the help of donor agencies, India should include the hemophilus influenza B and pneumococcal pneumonia vaccine in national UIP which will save millions of poor children's life.

Keywords: Hib, PCV13, rotavac, universal immunization program

Introduction

Immunization is the process whereby a person is made immune or resistant to an infectious disease, typically by the administration of a vaccine. Smallpox eradication program was successful in India in 1970 which drew the attention to the immunization program in India.^[1] The Expanded Program on Immunization (EPI) was flagged off in 1978 mainly in the urban areas for immunizing children <1 years age-group. Through the subsequent years, more vaccines were included in the program, e.g. oral polio vaccine (OPV) in 1979 and the vaccine to immunize pregnant mothers with tetanus toxoid (TT) vaccine in 1983. In 1985, the program was renamed as the Universal Immunization program (UIP) focusing mainly on infants and pregnant mothers. Measles vaccine was included in the program in 1990 and the

program had been expanded to spread across the country.^[2] UIP became a part of Child Survival and Safe Motherhood (CSSM) program in 1992 and then of Reproductive and Child Health (RCH) program in 1997.^[1,2] India included 2nd dose of measles in the national immunization program in 2010. Hepatitis B vaccination was included in UIP in 2002–2003 and in 2011 it covered whole over India. With the financial support from Global alliance for vaccine and immunization (GAVI), Indian government included Pentavac vaccine as a pilot project in few selected states in 2011.^[3] According to the recommendation of National technical advisory group of India (NATGI), Government of India are going to included four new vaccines for polio (injectable), rota virus, rubella, and japanese encephalitis (179 districts) in the UIP for whole India. So, at present UIP will fight against 10 vaccine preventable disease.^[4] Disease burden, safety, efficacy, cost-effectiveness, and operational requirements of the vaccination program are some of the important factors considered before including a vaccine

Access this article online

Quick Response Code:



Website:
www.jfmpc.com

DOI:
10.4103/2249-4863.152238

Address for correspondence: Dr. Jyotiranjana Sahoo,
Department of Community Medicine and Family Medicine,
All India Institute of Medical Sciences, Bhubaneswar, Sijua,
Dumduma, Odisha - 751 019, India.
E-mail: dr.jyotiranjana@gmail.com

in the national UIP. There are two more vaccines i.e. hemophilus influenza vaccine (Hib) and pneumococcal vaccine which are also relevant from Indian's prospective to fight against vaccine preventable diseases. In this present article, authors have tried to show a comparative descriptive analysis of the hemophilus influenza and pneumococcal pneumonia with rota virus, so that in near future Government of India can also consider their inclusion in the national UIP.

Why Hib or Pneumococcal Vaccine should be Included in UIP of India?

Hemophilus influenza type B (Hib) and streptococcus pneumoniae (pneumococcus) are the most common cause of pneumonia. Countries with high child mortality, pneumonia stands in front as a leading cause and United Nations International Children Emergency Fund (UNICEF), World Health Organization (WHO) has termed it as "Forgotten killers of children."^[32,33] Strategic advisory group of experts (SAGE) recommend that, countries with under five mortality rate >50 deaths/1000 births, or with >50 000 annual deaths among children, should make the introduction of conjugate pneumococcal vaccine a high priority for their immunization

programs.^[34] There were many challenges in front of the Indian government before introducing the rota viral vaccine in national UIP. But one of the biggest hindrances was solved because of introduction of low cost and effective indigenously developed rotavac vaccine. Many of the challenges of rota viral vaccine are same for Hib and pneumococcal vaccine. At this present juncture, India is not able to develop any indigenous vaccine against pneumonia but GAVI has promised to offer present PCV13 vaccine at a cost of 0.15–0.3 USD/dose for inclusion in the national immunization schedule.^[35] In future with the help of donor agencies like GAVI, World bank, WHO, UNICEF, Bill Gates Foundation, Indian government can think of introducing low cost Hib and pneumococcal pneumonia vaccine for national UIP. Promising experiences are available from different countries that had included Hib and pneumococcal vaccine into their routine immunization program. A study in Kenya showed after 3 year of introduction of Hib conjugate vaccine the incidence of invasive Hib disease declined drastically to 12% from baseline.^[36] Similar impact of the Hib vaccine within 5 years of its introduction into routine child immunization showed 65% decrease in absolute number of invasive H. Influenza diseases.^[37] Another impressive impact of Hib vaccine is that it provides herd immunity in the population.^[38,39] Similarly pneumococcal

Table 1: Comparative analysis of rota virus, hemophilus influenza, and streptococcus pneumonia in India

Characteristics of different diseases	Rota virus	Hemophilus influenza	Streptococcus pneumonia
Type of diseases in India	Diarrhea	Meningitis pneumonia	Meningitis, pneumonia, acute otitis media, bacteremia.
Proportional disease burden in India	Morbidity: 7-8% of community-based diarrhea episode. ^[5,6] Thirty-four percent of all diarrheal hospitalizations. ^[7] Mortality: 39.2% of all diarrheal deaths are due to rota virus. ^[8]	Morbidity: 2.4 million cases of sever disease due to Hib (2000). ^[9] Hib causing 13-19% of all pneumonia ^[10] and 25% of bacterial meningitis ^[11] (hospital-based study). Mortality: 72,000 deaths due to Hib.(2000) ^[9]	Morbidity: 12-35% of childhood pneumonia caused by streptococcus pneumoniae in India. ^[12] Mortality: Pneumococcal disease caused 1.3 million deaths in India. [10% of deaths in under 5 years age-group]. (2005) ^[13]
Type of strain present in India	G2P ^[4] and G1P ^[8] are the commonest serotypes. ^[14]	Mainly hemophilus influenza B	6A, 6B, 1, 19F, 19A, 14, 5, 7, 9V, 33,17are the commonest serotype. ^[15]
Type of vaccine available in India	Rotateq Roatrix ^[16] Rotavac (india's indedgius developed vaccine) ^[17]	Hemophilus influenza type B vaccine (Hib vaccine)	PCV 7, PCV10, PCV13 (latest recomm-entation) ^[15]
Vaccination schedule	Rotateq-3 doses (2, 4, and 6 month of age) ^[7] Rotarix-2 doses (2 and 4 month of age) ^[7] Rotavac-3 doses (6, 10, and 14 weeks of age) ^[18]	3 doses: 6, 10 and 14 week. ^[11]	3 doses: 6, 10, and 14 weeks and booster dose at 15 month. ^[19]
Efficacy level of vaccine	Rotarix protection level-58.3% ^[10] Rota Teq-48.1% ^[20] in India Rotavac-56% ^[21] in 1st year in India	More than 95% ^[11] in world including India.	PCV7: "3+1" schedule efficacy is 100% in South Africa, ^[22] 97.4% in California, ^[23] 93.9% in Netherland. ^[24] PCV13: 13 clinical trials in different part of the world have shown that PCV13efficacy is comparable to PCV7. ^[25] Acceptable level of safety ^[15]
Safety level of vaccine	Safe	Highly safe ^[26]	Acceptable level of safety ^[15]
Cost in India	Rotarix-US\$ 20.0/dose ^[21] Rotateq-US\$ 15.0/dose ^[27] Rotavac-US\$ 1.00/dose ^[28]	Hib-US\$ 5.83/dose ^[19]	PCV 13:-US\$ 69.9/dose. ^[19]
Cost-effectiveness analysis	Rotarix-In India, incremental cost-effectiveness ratio is US \$21.4 to US \$34per DALYs. ^[29] Rotavac-Cost-effectiveness is more than rotarix	In India, incremental cost-effectiveness ratio is US \$ 819 per DALYs. ^[30]	PCV 13-In Twain, incremental cost-effective ratio is US \$ 38,045 per DALYs. ^[31] In India no trail on cost-effectiveness

PCV: Pneumococcal vaccine; DALYs: Disability-adjusted life years

conjugate vaccine in USA, Canada, and Australia, both Invasive Pneumococcal Disease and pneumococcal pneumonia hospitalizations and deaths had decreased substantially.^[40-42] Pneumococcal vaccine gives protection not only against pneumonia but also other diseases like meningitis, otitis media, and bacteremia also.^[24] Globally 160 countries have included Hib vaccine in national immunization schedule.^[43] Indian government has already started inclusion of Hib vaccine (in the form of Pentavac) as pilot project in eight states (Tamil Nadu, Kerala, Haryana, Jammu and Kashmir, Gujarat, Karnataka, Goa, Pondicherry) of India.^[44] Given the experiences from other countries Hib and Pentavac should be considered for developing country like India. Introduction of Hib vaccination can be done through either scaling up the coverage of 'Pentavac vaccine' or introducing single shot Hib vaccine. But hindrances like financial burden and limitation of cold chain system should be looked after first before introducing new vaccine.^[45] Pentavac vaccine may be the answer to introduce new vaccine like Hib, without producing extra burden on the cold chain system. As the schedule of Pentavac, Hib and pneumococcal vaccine are same with the present vaccination schedule under UIP, introduction of new vaccines will not increase the visit to health facility which in turn will not affect the cost and coverage of the programme. Table 1 shows the comparison between Rota virus, Hemophilus influenza and Streptococcus pneumonia in India.

Conclusion

Inclusion of rota viral vaccine in spite of all the challenges in national immunization schedule is one of the major commitments of India against vaccine preventable diseases (VPDs). Indigenously developed rota viral vaccine (rotavac) was a result of a public-private partnership between Ministry of health and family welfare, Ministry of science and technology, and Bharat Biotech.^[4] India need more trail on the serotype specificity, efficacy, and cost-effectiveness before including pneumococcal vaccine in UIP. Present burden of hemophilus influenza and pneumococcal disease are not less than rota viral disease and vaccine efficacy and safety level are also above the level of WHO criteria to include it into a public health program. So, policy makers in India should consider including Hib vaccine (alone or Pentavac) and pneumococcal vaccine in national UIP to save life of millions of poor children.

References

1. Patra N. "When will they ever learn?"The great Indian experience of Universal Immunization Programme [dissertation]. New Delhi (ND): Centre for economic studies and planning, School of social Sciences, Jawaharlal Nehru University; 2009.
2. Khera A, Gupta A, Gogia H, Rao S. India's national immunization programme [Internet]. New Delhi: Seminar Publication; 2012. Available from: http://www.india-seminar.com/2012/631/631_ajay_khera_et_at.html [Last cited 2014 Aug 5].
3. Lahariya C. A brief history of vaccines and vaccination in India. *Indian J Med Res* 2014;491-551.

4. Datta J. Four vaccines added to India's immunization programme. *The Hindu*; 2014.
5. Parashar UD, Gibson CJ, Bresse JS, Glass RI. Rotavirus and severe childhood diarrhoea. *Emerg Infect Dis* 2006;12:304-6.
6. Banerjee I, Ramani S, Primrose B, Moses P, Iturriza G M, Gray JJ, *et al*. Comparative study of the epidemiology of rotavirus in children from a community-based birth cohort and a hospital in South India. *J Clin Microbiol* 2006;44:2468-74.
7. Khan G, Fitzwater S, Tate J, Kang G, Ganguly N, Nair G, *et al*. Epidemiology and prospect for prevention of rotavirus disease in India. *Indian Pediatr* 2012;49:467-74.
8. Parashar UD, Hummelman EG, Bresee JS, Miller MA, Glass RI. Global illness and deaths caused by rotavirus disease in children. *Emerg Infect Dis* 2003;9:565-72.
9. Watt JP, Wolfson LJ, O'Brien KL, Henkle E, Deloria-Knoll M, McCall N, *et al*. Burden of disease caused by Haemophilus influenzae type b in children younger than 5 years: Global estimates. *Lancet* 2009;374:903-11.
10. Bahl R, Mishra S, Sharma D, Singhal A, Kumari S. A bacteriological study in hospitalized children with pneumonia. *Ann Trop Paediatr* 1995;15:173-7.
11. Subcommittee on Introduction of Hib Vaccine in Universal Immunization Program, National Technical Advisory Group on Immunization, India. NATGI subcommittee recommendations on haemophilus influenzae type B (Hib) vaccine introduction in India. *Indian Pediatr* 2009;46:945-54.
12. Mathew JL, Patwari AK, Gupta P, Shah D, Gera T, Gogai S, *et al*. Acute respiratory infection and pneumonia in India: A systematic review of literature for advocacy and action: UNICEF-PHFI Series on newborn and child health, India. *Indian Pediatr* Mar 2011;48:191-218.
13. Johnson HL, Diego GB, Jamie P, Orin SL, Thomas C, Katherine LO. Burden of childhood mortality caused by streptococcus pneumonia in India. Available from: http://www.jhsph.edu/research/centers-and-institutes/ivac/resources/isppd8/H_Johnson_Burden_of_Child_Mortality_by_Strep_Pneumo_in_India.pdf [Last cited on 2014 Jul 5].
14. Kang G, Arora R, Chitambar SD, Deshpande J, Gupte MD, Kulkarni M, *et al*. Multicenter, hospital-based surveillance of rotavirus disease and strains among Indian Children Aged <5 Years. *J Infect Dis* 2009;200 Suppl 1:S147-53.
15. Malik A, Taneja D. Conjugate pneumococcal vaccines: Need and choice in India. *Indian J Community Med* 2013;38:189-91.
16. Narang A, Bose A, Pandit AN, Dutta P, Kang G, Bhattacharya SK, *et al*. Immunogenicity, reactogenicity and safety of human rotavirus vaccine (RIX4414) in Indian infants. *Hum Vaccin* 2009;5:414-9.
17. Bhandari N, Sharma P, Taneja S, Kumar T, Rongsen-Chandola T, Appaiahgari MB, *et al*; Rotavirus Vaccine Development Group. A dose-escalation safety and immunogenicity study of live attenuated oral rotavirus vaccine 116E in infants: A randomized, double-blind, placebo-controlled trial. *J Infect Dis* 2009;200:421-9.
18. Jha DN. Now a desi rotavirus vaccine. *The Times of India*; 2013.
19. Netvag.org [Internet]. Cost guide to immunization; c 2011. Available from: <http://www.nextvac.org/vaccination.html> [Last cited on 2014 Jul 12].
20. Vesikari T, Karvonen A, Prymula R, Schuster V, Tejedor JC, Cohen R, *et al*. Efficacy of human rotavirus vaccine against rotavirus gastroenteritis during the first 2 years of life in

- European infants: Randomized, double blind controlled study. *Lancet* 2007;370:1757-63.
21. Sharma EK. India-made, low-cost rotavirus vaccine likely by 2014. *Business Today*; 2013.
 22. Madhi SA, Cohen C, von Gottberg A. Introduction of pneumococcal conjugate vaccine into the public immunization program in South Africa: Translating research into policy. *Vaccine* 2012;30:C21-7.
 23. Nuorti JP, Whitney CG; Centers for Disease, Control and Prevention (CDC). Prevention of pneumococcal disease among infants and children: Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2010;59:1-18.
 24. Vemer P, Greeff S C, Schouls LM, Maiwenn AI, Melker H E. The cost-utility of infant vaccination with a 7, 10 and 13 valent pneumococcal conjugate vaccine in the Netherlands. *Value Health* 2009;12:A228.
 25. Paradise PR. Advances in pneumococcal disease prevention: 13-valent pneumococcal conjugate vaccine for infants and children. *Clin Infect Dis* 2011;52:1241-7.
 26. Acharya D, Bhave S, Joshi V, Bavdekar A, Pandit A. Haemophilus influenzae type b vaccine in India: Need and timing, immunogenicity and tolerance. *Indian Pediatr* 1997;34:9-15.
 27. MSD launches diarrhoea vaccine 'RotaTeq' in India. *The Hindu*; 2011
 28. Rotavirus Vaccine Developed in India Demonstrates Strong Efficacy. *ANI- Business Wire India* 2013. p. 14.
 29. Rose J, Hawthorn RL, Watts B, Singer ME. Public health impact and cost effectiveness of mass vaccination with live attenuated human rotavirus vaccine (RIX4414) in India: Model based analysis. *BMJ* 2009;339:b3653.
 30. Gupta M, Prinja S, Kumar R, Kaur M. Cost-effectiveness of Haemophilus influenza type b (Hib) vaccine introduction in the universal immunization schedule in Haryana State, India. *Health Policy Plan* 2013;28:51-61.
 31. Wu DB, Chang CJ, Huanq YC, Wen YW, Wu CL, Fann CS. Cost-effectiveness analysis of pneumococcal conjugate vaccine in Taiwan: A transmission dynamic modeling approach. *Value Health* 2012;15 Suppl 1:S 15-19.
 32. Madhi SA, Levine OS, Hajjeh R, Mansoor OD, Cherian T. Vaccines to prevent pneumonia and improve child survival. *Bull World Health Organ* 2008;86:365-72.
 33. Pneumonia: The forgotten killer of children. Geneva: UNICEF/WHO; 2006.
 34. World Health Organization. Weekly epidemiological record, no 12. Available from: http://www.who.int/wer/2007/wer8201_02.pdf [Last cited on 2007 Jan 12].
 35. Verma R, Khanna P. Pneumococcal conjugate vaccine: A newer vaccine available in India. *Hum Vacc Immunother* 2012;8:1317-20.
 36. Cowgill KD, Ndiritu M, Nyiro J, Slack MP, Chiphatsi S, Ismail A, *et al.* Effectiveness of Haemophilus influenzae type b Conjugate vaccine introduction into routine childhood immunization in Kenya. *JAMA* 2006;296:671-8.
 37. von Gottberg A, de Gouveia L, Madhi SA, Du Plessis M, Quan V, Soma K, *et al.* Impact of conjugate Haemophilus influenza type b (Hib) vaccine introduction in South Africa. *Bull World Health Organ* 2006;84:811-8.
 38. Takala AK, Eskola J, Leinonen M, Käyhty H, Nissinen A, Pekkanen E, *et al.* Reduction of oropharyngeal carriage of Haemophilus influenzae type b (Hib) in children immunized with Hib conjugate vaccine. *J Infect Dis* 1991;164:982-6.
 39. Murphy TV, Pastor P, Medley R, Osterholm MT, Granoff DM. Decreased Haemophilus colonization in children vaccinated with Haemophilus influenzae type b conjugate vaccine. *J Pediatr* 1993;122:517-23.
 40. Simonsen L, Taylor RJ, Young-Xu Y, Haber M, May L, Klugman KP. Impact of pneumococcal conjugate vaccination of infants on pneumonia and influenza hospitalization and mortality in all age groups in the United States. *MBio* 2011;2:e00309-10.
 41. Kellner JD, Vanderkooi OG, MacDonald J, Church DL, Tyrrell GJ, Scheifele DW. Changing epidemiology of invasive pneumococcal disease in Canada, 1998-2007: Update from the Calgary-area Streptococcus pneumoniae research (CASPER) study. *Clin Infect Dis* 2009;49:205-12.
 42. Roche PW, Krause V, Cook H, Barralet J, Coleman D, Sweeny A, *et al.*; Enhanced Invasive Pneumococcal Disease Surveillance Working Group; Pneumococcal Working Party of the Communicable Diseases Network Australia. Invasive pneumococcal disease in Australia, 2006. *Commun Dis Intell Q Res* 2008;32:18-30.
 43. Vemer P, Greeff SC, Schouls LM, Maiwenn AI, Melker HE. The cost-utility of infant vaccination with a 7, 10 and 13 valent pneumococcal conjugate vaccine in the Netherlands. *Value Health* 2009;12:A228.
 44. Universal immunization programme. Ministry of health and family welfare. Available from: <http://mohfw.nic.in/index 1.php? lang = 1 and level = 2 and sublinkid = 2759 and lid = 1882> [Last cited 2014 Aug 10].
 45. Hyde TB, Dentz H, Wang SA, Burchett HE, Mounier-Jack S, Mantel CF, *et al.*; New Vaccine Introduction Impact Published Literature Working Group. The impact of new vaccine introduction on immunization and health systems: A review of the published literature. *Vaccine* 2012;30:6347-58.

How to cite this article: Paul S, Sahoo J. Four new vaccines for routine immunization in India: What about hemophilus influenza B and pneumococcal vaccine?. *J Fam Med Primary Care* 2015;4:9-12.

Source of Support: Nil. **Conflict of Interest:** None declared.